

Appl. No.: 10/658,241
Reply to Office Action of May 24, 2005

Amendments to the Claims

This listing of claims will replace all prior listings in this application.

Claims 1-16 (canceled)

Claim 17 (currently amended) The process of Claim 45 42 or 46 43, wherein the oligomers are 5, 7, 3', 4'-tetra-O-benzyl-protected-(4 β ,8) epicatechin-oligomers, and wherein the silver tetrafluoroborate is dried before the reaction.

Claim 18 (pending) The process of Claim 17, wherein the drying is vacuum drying carried out immediately before the reaction.

Claim 19 (currently amended) The process of Claim 46 43, wherein the mixture comprises protected trimer through protected heptamer when the protected oligomer is the protected dimer, protected tetramer through protected octamer when the protected oligomer is the protected trimer, and the protected pentamer through the protected undecamer when the protected oligomer is the protected tetramer.

Claim 20 (currently amended): The process of Claim 46 43, further comprising the step of isolating the protected oligomers in the mixture by reverse phase high pressure liquid chromatography.

Claim 21 (currently amended) The process of Claim 20, further comprising the step of removing the acetyl-protecting group(s) groups from the isolated oligomers.

Claim 22 (currently amended) The process of Claim 21, where the acetyl-protecting group(s) groups are removed with aqueous tetra-n-butyl ammonium hydroxide.

Claim 23 (pending) The process of Claim 20, further comprising the step of removing the benzyl-protecting groups from the isolated oligomers.

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Claim 24 (pending) The process of Claim 23, wherein the benzyl-protecting groups are removed by hydrogenolysis.

Claim 25 (currently amended) The process of Claim 20, further comprising the steps of removing the acetyl-protecting groups and then removing the benzyl protecting groups.

Claim 26 (currently amended) The process of Claim 25, wherein the acetyl-protecting group(s) groups are removed with aqueous tetra-n-butyl ammonium hydroxide and wherein the benzyl-protecting groups are removed by hydrogenolysis.

Claim 27 (withdrawn) A process for preparing a mixture of 5,7,3',4'-tetra-O-benzyl-epicatechin-(4 β ,8)-oligomers comprises the steps of:

(a) activating the C-4 position of 5,7,3',4'-tetra-O-benzyl-epicatechin with a 2-(benzothiazolyl)thio group to form 4-[(2-benzothiazolyl)thio]-5, 7, 3', 4'-tetra-O-benzylepicatechin; and

(b) self-condensing the 4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzylepicatechin in the presence of silver tetrafluoroborate or an acidic clay.

Claim 28 (withdrawn) The process of Claim 27, further comprising the steps of separating the oligomers and removing the benzyl groups.

Claim 29 (withdrawn) A process for chain extending a protected epicatechin (4 β ,8) oligomer with a C-4 activated, protected epicatechin (4 β ,8) oligomer comprises the step of condensing an epicatechin (4 β ,8)-oligomer having acetyl protecting groups at the 3-positions of all mers, benzyl protecting groups at the 5, 7, 3' and 4' positions of all mers, and having a C-4-[2-(benzothiazolyl)thio] activating group on a terminal mer with an epicatechin oligomer having acetyl protecting groups at the 3-positions of each

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mer and benzyl protecting groups at the 5, 7, 3' and 4' positions of each mer in the presence of silver tetrafluoroborate or an acidic clay.

Claim 30 (withdrawn) The process of Claim 29, wherein one of the C-4 activated, protected oligomers is 3-O-acetyl-5,7,3',4'-tetra-O-benzyl-epicatechin-(4 β ,8)-3-O-acetyl-4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzyl-epicatechin; wherein the benzyl-protected oligomer is tetrakis (3-O-acetyl-5,7,3',4'-tetra-O-benzyl)epicatechin (4 β ,8)₃-tetramer; wherein the protected, chain-extended oligomer is hexakis (3-O-acetyl-5,7,3',4'-tetra-O-benzyl)epicatechin (4 β ,8)₅-hexamer.

Claim 31 (withdrawn) 4-[(2-Benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzyl-epicatechin or 4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzyl-catechin.

Claim 32 (withdrawn) A process for preparing the 4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzyl-epicatechin of Claim 31 comprises reacting 5,7,3',4'-tetra-O-benzyl-4-(2-hydroxyethoxy)-epicatechin with an organoaluminum thiolate generated from 2-mercaptobenzothiazole.

Claim 33 (withdrawn) 4-[(2-Benzothiazolyl)thio]-3-O-acetyl-5,7,3',4'-tetra-O-benzyl-epicatechin or 4-[(2-benzothiazolyl)thio]-3-O-acetyl-5,7,3',4'-tetra-O-benzyl-catechin.

Claim 34 (withdrawn) A process for preparing the 4-[(2-benzothiazolyl)thio]-3-O-acetyl-5,7,3',4'-tetra-O-benzyl-epicatechin of Claim 33 comprises reacting 5,7,3',4'-tetra-O-benzyl-4-(2-hydroxyethoxy)-epicatechin with an organoaluminum thiolate generated from 2-mercaptobenzothiazole followed by acetylation.

Claim 35 (withdrawn) A process for preparing a (4 β ,8)-dimer comprises the step of reacting (4-(benzylthio)epicatechin or 4-(benzylthio)catechin with epicatechin or

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catechin in the presence of silver tetrafluoroborate or dimethyl (methylthio) sulfonium tetrafluoroborate.

Claim 36 (withdrawn) 4-(Benzylthio)epicatechin or 4-(benzylthio)catechin.

Claim 37 (withdrawn) A process for preparing the compound of Claim 36 comprises reacting epicatechin or catechin with benzyl ~~mercaptan~~ mercaptan.

Claim 38 (withdrawn) A method of treating breast cancer in a mammal in need of such treatment, which treatment inhibits cancer cell growth through cell cycle arrest in the Go/G phase and comprises administering to the mammal epicatechin-(4,8)₄-pentamer, wherein the breast cancer cells are selected from the group consisting of human breast cancer cell lines MCF-7, SKBR-3, MDA 435, and MDA MB-231.

Claim 39 (withdrawn) The method of Claim 38, wherein the pentamer is a purified procyanidin fraction isolated from cocoa beans as a cocoa extract.

Claim 40 (withdrawn) The method of Claim 39, wherein the pentamer is a synthetically prepared procyanidin.

Claim 41 (withdrawn) The method of Claim 39, wherein the breast cancer cells are from the MDA MB-231 cell line.

Claim 42 (new) A process for preparing a mixture of 5, 7, 3', 4'-tetra-O-benzyl-epicatechin-(4,8)-oligomers comprises reacting a 5, 7, 3', 4'-tetra-O-benzyl-epicatechin or -catechin monomer or a 5, 7, 3', 4'-tetra-O-benzyl-epicatechin or -catechin-(4,8)-oligomer with a 3-O-acetyl-4-[(2-benzothiazolyl)thio]-5, 7, 3', 4'-tetra-O-benzyl-epicatechin or -catechin monomer in the presence of silver tetrafluoroborate.

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Claim 43 (new) A process for preparing a mixture of 3-O-acetyl-5, 7, 3', 4'-tetra-O-benzyl-epicatechin- and/or -catechin-(4,8)-oligomers comprises reacting a 3-O-acetyl-5, 7, 3', 4'-tetra-O-benzyl-epicatechin or -catechin monomer or a 3-O-acetyl-5, 7, 3', 4'-tetra-O-benzyl-epicatechin- and/or -catechin-(4,8)-oligomer with a 3-O-acetyl-4-[(2-benzothiazolyl)thio]-5, 7, 3', 4'-tetra-O-benzyl-epicatechin or -catechin monomer in the presence of silver tetrafluoroborate.

Claim 44 (new) The process of Claim 15, further comprising the step of isolating the protected oligomers in the mixture by reverse phase high pressure liquid chromatography.

Claim 45 (new) The process of Claim 44, further comprising the step of removing the benzyl-protecting groups from the isolated oligomers. The process of Claim 44, further comprising the step of removing the benzyl-protecting groups from the isolated oligomers.

Claim 46 (new) The process of Claim 45, wherein the benzyl-protecting groups are removed by hydrogenolysis. The process of Claim 23, wherein the benzyl-protecting groups are removed by hydrogenolysis.